L Number	Hits	Search Text	DB	Time stamp
2	708944	neovascularization or angiogen$6 or capillary or vessel$3 or vascularization	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/10/29 16:00
3	289121	eye or ocula$5 or intraocular	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/10/29 15:46
5	9281	(neovascularization or angiogen$6 or capillary or vessel$3 or vascularization) SAME (eye or ocula$5 or intraocular)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/10/29 15:46
6	35424	(neovascularization or angiogen$6 or capillary or vessel$3 or vascularization) and (eye or ocula$5 or intraocular)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/10/29 15:47
7	20185	(retrovir$5 or lentivir$5 or Moloney or HIV) WITH vector$3	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/10/29 15:59
8	4335	((retrovir$5 or lentivir$5 or Moloney or HIV) WITH vector$3) and ((neovascularization or angiogen$6 or capillary or vessel$3 or vascularization) and (eye or ocula$5 or intraocular))	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/10/29 15:51
9	3835	(((retrovir$5 or lentivir$5 or Moloney or HIV) WITH vector$3) and ((neovascularization or angiogen$6 or capillary or vessel$3 or vascularization) and (eye or ocula$5 or intraocular))) and (gene ADJ thera$5)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/10/29 15:51
12	521	((((retrovir$5 or lentivir$5 or Moloney or HIV) WITH vector$3) and ((neovascularization or angiogen$6 or capillary or vessel$3 or vascularization) and (eye or ocula$5 or intraocular))) and (gene ADJ thera$5)) and (macular ADJ degeneration)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/10/29 15:53
13	3340	(neovascularization or angiogen$6) SAME (eye or ocular or intraocular)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/10/29 16:21
14	637	((neovascularization or angiogen$6) SAME (eye or ocular or intraocular)) and ((retrovir$5 or lentivir$5 or Moloney or HIV) WITH vector$3)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/10/29 16:04
15	9	((neovascularization or angiogen$6) SAME (eye or ocular or intraocular)) SAME ((retrovir$5 or lentivir$5 or Moloney or HIV) WITH vector$3)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/10/29 16:05
19	2	Appukuttan NEAR Binoy	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/10/29 16:07
22	4	Stout NEAR Timothy	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/10/29 16:08
23	174	(neovascularization) SAME intraocular	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/10/29 16:21
24	24	((neovascularization) SAME intraocular) and ((retrovir$5 or lentivir$5 or Moloney or HIV) WITH vector$3)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/10/29 16:27
25	30203	Monokine ADJ induced ADJ by interferon$9	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/10/29 16:29

26	3	((neovascularization) SAME intraocular) and (MIG or IP10)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/10/29 16:33
27	172	ocular SAME gene ADJ therapy	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/10/29 16:33
28	18	(ocular SAME gene ADJ therapy) and (((neovascularization or angiogen$6) SAME (eye or ocular or intraocular)) and ((retrovir$5 or lentivir$5 or Moloney or HIV) WITH vector$3))	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/10/29 16:34
29	18	(US-6397849-$ or US-6489305-$).did. or (US-20020114783-$ or US-20020183253-$ or US-20030045498-$ or US-20030082159-$ or US-20020137678-$ or US-20030100497-$ or US-20030105011-$ or US-20030105012-$ or US-20030109438-$ or US-20030105013-$ or US-20030113870-$ or US-20030125521-$ or US-20030119112-$ or US-20030158112-$ or US-20030105055-$ or US-20030191072-$).did.	USPAT; US-PGPUB	2003/10/29 16:40

(FILE 'HOME' ENTERED AT 16:40:13 ON 29 OCT 2003)

FILE 'MEDLINE' ENTERED AT 16:40:25 ON 29 OCT 2003
L1 135 S GENE THERAPY (L) (EYE OR OCULAR OR INTRAOCULAR)
L2 342617 S NEOVASCULAR? OR VASCULAR? OR ANGIOGEN?
L3 22 S L1 AND L2
L4 22 SORT L3 PY
L5 33122 S LENTIVIR? OR RETROVIR?
L6 5 S L1 AND L2 AND L5
L7 1397 S MONOKINE-INDUCED? OR MIG OR INTERFERON?(W)INDUCIBLE OR IP10
L8 0 S L7 AND L1
L9 13 S L7 AND (EYE OR OCULAR OR INTRAOCULAR)
L10 1 S L9 AND (NEOVASCULAR? OR VASCULAR? OR ANGIOGEN?)
L11 1987 S MONOKINE-INDUCED? OR MIG OR INTERFERON?(W)INDUCIBLE OR IP-10
L12 1 S L11 AND (EYE OR OCULAR OR INTRAOCULAR)(L)(NEOVASCULAR? OR VAS
L13 33 S L11 AND (GENE THERAPY)
L14 33 SORT L13 PY

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED AT 16:58:22 ON 29 OCT 2003
L15 32 S L6
L16 9 S L12
L17 21 DUP REM L15 (11 DUPLICATES REMOVED)
L18 6 DUP REM L16 (3 DUPLICATES REMOVED)
L19 21 SORT L17 PY
L20 6 SORT L18 PY
E APPUKUTTAN BINOY/AU
E TIMOTHY STOUT?/AU
E APPUKUTTAN BINOY/AU
L21 16 S E3
L22 218140 S HIS
L23 9 S L21 AND (OCULAR OR INTRAOCULAR OR EYE)
L24 9 SORT L23 PY

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L24 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:334392 CAPLUS
DN 138:348751
TI Lentiviral vector-mediated gene transfer and uses thereof
SO U.S. Pat. Appl. Publ., 61 pp., Cont.-in-part of U. S. Ser. No. 25,264.
CODEN: USXXCO
IN **Appukuttan, Binoy**; Stout, J. Timothy
AB The present invention provides lentiviral vectors that are useful in human gene therapy for inherited or acquired proliferative **ocular** disease. It furnishes methods to exploit the ability of lentiviral vectors to transduce both mitotically active and inactive cells so that **eye** diseases may be treated.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003082159	A1	20030501	US 2002-245050	20020917
	US 2002114783	A1	20020822	US 2001-25264	20011219

L24 ANSWER 6 OF 9 MEDLINE on STN
AN 2003194940 MEDLINE
TI Corneal transduction to inhibit angiogenesis and graft failure.
SO INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, (2003 May) 44 (5) 1837-42.
Journal code: 7703701. ISSN: 0146-0404.
AU Murthy Raghu C; McFarland Trevor J; Yoken Jon; Chen Sandy; Barone Chris; Burke Dorthea; Zhang Yi; **Appukuttan Binoy**; Stout J Timothy
AB PURPOSE: To test whether lentivirus-mediated expression of an endostatin::kringle-5 (E::K-5) fusion gene has an inhibitory effect on neovascularization and failure of corneal transplants. METHODS: A lentiviral vector containing a fusion transgene comprising the human endostatin gene and the kringle-5 domain of the human plasminogen gene (E::K-5) was used for transduction of corneal buttons ex vivo. The corneal buttons were transplanted after overnight incubation in media containing either lentivirus or PBS. Sixteen rabbits underwent allogenic penetrating keratoplasty in one **eye**. The area of neovascularization from the limbus to within the graft was documented

after surgery. RT-PCR was performed to demonstrate the presence of transgene mRNA within the graft. Histopathology was used to analyze neovascularization, inflammation, and rejection morphology. RESULTS: Less neovascularization was observed in corneas treated with the lentivirus E::K-5 fusion vector. Early onset and profound neovascularization was observed in control **eyes**. E::K-5-treated animals did not have graft failure, whereas five of the six control animals had graft failure, as classified by opacification of the graft. All E::K-5 transduced corneas tested were positive by RT-PCR for the unique fusion gene sequence. Histopathology corroborated a significant increase of blood vessel presence and inflammatory reaction in control compared with treated **eyes**. CONCLUSIONS: Corneas transduced with a lentivirus containing an endostatin::kringle-5 fusion gene demonstrated an inhibition of neovascularization and graft failure. E::K-5 gene transduction through a lentiviral vector system may be a useful adjunct to prevent graft neovascularization and corneal graft rejection in high-risk corneal transplants with antecedent rejection or neovascularization.

L24 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:487422 CAPLUS
DN 137:57587
TI Lentiviral vector-mediated gene transfer and uses thereof
SO PCT Int. Appl., 91 pp.
CODEN: PIXXD2
IN Stout, J. Timothy; **Appukuttan, Binoy**
AB The present invention provides a means of human gene therapy for inherited or acquired proliferative **ocular** disease. It furnishes methods to exploit the ability of lentiviral vectors to transduce both mitotically active and inactive cells so that **eye** diseases may be treated.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002049677	A1	20020627	WO 2001-US49241	20011218
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002034053	A5	20020701	AU 2002-34053	20011218
EP 1343532	A1	20030917	EP 2001-985065	20011218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

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L1 135 S GENE THERAPY (L) (EYE OR OCULAR OR INTRAOCULAR)
L2 342617 S NEOVASCULAR? OR VASCULAR? OR ANGIOGEN?
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L9 13 S L7 AND (EYE OR OCULAR OR INTRAOCULAR)
L10 1 S L9 AND (NEOVASCULAR? OR VASCULAR? OR ANGIOGEN?)
L11 1987 S MONOKINE-INDUCED? OR MIG OR INTERFERON?(W)INDUCIBLE OR IP-10
L12 1 S L11 AND (EYE OR OCULAR OR INTRAOCULAR)(L)(NEOVASCULAR? OR VAS
L13 33 S L11 AND (GENE THERAPY)
L14 33 SORT L13 PY

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED AT 16:58:22 ON 29 OCT 2003
L15 32 S L6
L16 9 S L12
L17 21 DUP REM L15 (11 DUPLICATES REMOVED)
L18 6 DUP REM L16 (3 DUPLICATES REMOVED)
L19 21 SORT L17 PY
L20 6 SORT L18 PY

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L19 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:487422 CAPLUS
DN 137:57587
TI **Lentiviral** vector-mediated gene transfer and uses thereof
SO PCT Int. Appl., 91 pp.
CODEN: PIXXD2
IN Stout, J. Timothy; Appukuttan, Binoy
AB The present invention provides a means of human **gene therapy** for inherited or acquired proliferative **ocular** disease. It furnishes methods to exploit the ability of **lentiviral** vectors to transduce both mitotically active and inactive cells so that **eye** diseases may be treated.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002049677	A1	20020627	WO 2001-US49241	20011218
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002034053	A5	20020701	AU 2002-34053	20011218
EP 1343532	A1	20030917	EP 2001-985065	20011218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

L19 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:606326 CAPLUS
DN 139:172876
TI Can we treat diabetic retinopathy with gene therapy?
SO Atarashii Ganka (2003), 20(7), 909-917
CODEN: ATGAEX; ISSN: 0910-1810
AU Mori, Keisuke
AB A review on the current status of **gene therapy**, treatment of retinal pigmentary degeneration model using ribozyme, characteristics of viral vectors (retro-, adeno-, adeno-assocd.-, and

lentiviral), **gene therapy** of age-related macular degeneration by pigment epithelium-derived factor (PEDF) gene, inhibition of **ocular neovascularization** and protection of retinal cells by adenoviral vector carrying PEDF gene (AdPEDF.11), and possible treatment of diabetic retinopathy by AdPEDF.11.

L19 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:334392 CAPLUS
DN 138:348751
TI **Lentiviral** vector-mediated gene transfer and uses thereof
SO U.S. Pat. Appl. Publ., 61 pp., Cont.-in-part of U. S. Ser. No. 25,264.
CODEN: USXXCO
IN Appukuttan, Binoy; Stout, J. Timothy
AB The present invention provides **lentiviral** vectors that are useful in human **gene therapy** for inherited or acquired proliferative **ocular** disease. It furnishes methods to exploit the ability of **lentiviral** vectors to transduce both mitotically active and inactive cells so that **eye** diseases may be treated.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2003082159	A1	20030501	US 2002-245050	20020917
US 2002114783	A1	20020822	US 2001-25264	20011219

L19 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:91922 CAPLUS
DN 139:47076
TI **Lentivirus**-mediated expression of angiostatin efficiently inhibits **neovascularization** in a murine proliferative retinopathy model
SO Gene Therapy (2003), 10(3), 219-226
CODEN: GETHEC; ISSN: 0969-7128
AU Igarashi, Tsutomu; Miyake, Koichi; Kato, Ko; Watanabe, Atsushi; Ishizaki, Masamichi; Ohara, Kunitoshi; Shimada, Takashi
AB Ischemic retinal diseases, such as diabetic retinopathy, retinopathy of prematurity, and age-related macular degeneration, are a major cause of blindness worldwide. Angiostatin is an internal peptide fragment of plasminogen that inhibits endothelial proliferation in vitro and tumor growth in vivo. We now demonstrate that HIV vector encoding angiostatin (HIV-angiostatin) can inhibit retinal **neovascularization** in a mouse model of proliferative retinopathy. Intravitreal injections of HIV-angiostatin led to stable expression of the angiostatin gene in retinal tissue. Retinal **neovascularization** was histol. quantitated by a masked protocol. Retinal **neovascularization** in the eye injected with HIV-angiostatin was reduced in 90% (9/10; P=0.025) of animals, compared with the eye injected with phosphate-buffered saline. Redn. of histol. evident **neovascular** nuclei per 6-.mu.m section averaged 68%, with maximal inhibitory effects of 87%. **Neovascularization** was not reduced in the eyes injected with HIV vector encoding enhanced green fluorescent protein. This is the first report that HIV-angiostatin can reduce **neovascular** cell nuclei in a murine proliferative retinopathy model. These data suggest that the anti-**angiogenic** activity of angiostatin has therapeutic potential for the treatment of retinal **neovascularization**.

L19 ANSWER 2 OF 21 MEDLINE on STN
AN 97465002 MEDLINE
TI **Ocular gene therapy**: experimental studies and clinical possibilities.
SO OPHTHALMIC RESEARCH, (1997) 29 (5) 242-51. Ref: 22
Journal code: 0267442. ISSN: 0030-3747.
AU Murata T; Kimura H; Sakamoto T; Osusky R; Spee C; Stout T J; Hinton D R; Ryan S J
AB The Human Genome Project will identify, map and sequence all 50,000-100,000 human genes and will provide the tools to determine the genetic basis of both common and rare diseases. Understanding the genetic basis of human disease will allow for the development of highly specific drugs and for replacement of the altered gene through **gene therapy**. **Gene therapy** may also be used to introduce a new function into cells with resulting therapeutic benefit. Genes may be delivered into cells in vitro or in vivo utilizing viral or

nonviral vectors. Viral vectors which have been used include **retroviruses**, adenoviruses, adeno-associated viruses and herpes viruses. **Ocular** disorders with the greatest potential for benefit of **gene therapy** at the current time include hereditary **ocular** diseases, including retinitis pigmentosa, tumors such as retinoblastoma or melanoma, and acquired proliferative and **neovascular** retinal disorders. We have demonstrated the feasibility of **ocular gene therapy** in a rabbit model of proliferative vitreoretinopathy, using **retroviral** vectors containing the herpes simplex virus thymidine kinase 'suicide' gene. Although in vivo transduction efficiency is low, the strong bystander effect results in prominent killing of proliferating cells in this model leading to inhibition of disease. In the future, **gene therapy** has the potential for the replacement of defective gene products or introduction of new gene products into **ocular** cells. The selection of appropriate target genes and cells will be critical, as will the development of a methodology for safe, targeted gene transfer.

L19 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:684243 CAPLUS
DN 127:326576
TI **Gene therapy** for proliferative vitreoretinopathy and other **ocular** disorders involving **intraocular** cellular proliferation
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
IN Hinton, David; Anderson, W. French; Ryan, Stephen J.; Stout, J. Timothy
AB A method is disclosed for treating ocular disorders (e.g. proliferative vitreoretinopathy) assocd. with replicating ocular cells. Th method includes transfecting replicating ocular cells in vivo with a polynucleotide encoding an agent which is capable of providing for the inhibition, prevention, or destruction of the growth of the replicating ocular cells upon expression of the agent. The agent may be a viral thymidine kinase, and the polynucleotide encoding the agent may be contained in a **retroviral** vector. Once the replicating ocular cells are transduced with the **retroviral** vector, the patient is given a chemotherapeutic or interaction agent, e.g. ganciclovir, which kills the transfected replicating ocular cells.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9737542	A1	19971016	WO 1997-US5699	19970408
W: AU, CA, JP, NZ, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9724431	A1	19971029	AU 1997-24431	19970408
AU 726584	B2	20001109		
EP 954222	A1	19991110	EP 1997-920169	19970408
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000510449	T2	20000815	JP 1997-536394	19970408
US 2003191072	A1	20031009	US 1998-174210	19981016

L19 ANSWER 4 OF 21 MEDLINE on STN
AN 1999019302 MEDLINE
TI **Retrovirus**-mediated gene transfer to photocoagulation-induced choroidal **neovascular** membranes.
SO INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, (1998 Nov) 39 (12) 2474-8.
Journal code: 7703701. ISSN: 0146-0404.
AU Murata T; Hangai M; Ishibashi T; Spee C; Gordon E M; Anderson W F; Hinton D R; Ryan S J
AB PURPOSE: To determine the feasibility of experimental gene transfer to laser-induced choroidal **neovascular** membrane (CNVM) in rats, with a **retroviral** vector containing the reporter construct beta-galactosidase (beta-gal). METHODS: Laser photocoagulation was used to induce CNVM in rats. To ascertain the duration of beta-gal expression in the CNVM, 23 rats received 10 burns (75 microm, 100 mW, 0.1 seconds) in their right **eyes**, and beta-gal expression was examined from day 3 to 4 months. In addition, 14 pigmented rats were treated with 3 photocoagulation burns in their right **eyes**. beta-gal vector was injected into the vitreous or subretinal space 2 days later. On day 14, fluorescein angiography was performed to detect choroidal

neovascularization. Then, beta-gal expression in each photocoagulation-induced CNVM was examined by observing the exposed fundus of the **eyes** stained with the beta-gal substrate X-Gal. RESULTS: beta-gal expression was identified in the CNVM induced by photocoagulation from day 5 (16.2% +/- 6.8% of the lesions) to 4 months (3.7% +/- 2.4%). Histopathologic examination revealed beta-gal-transduced macrophages and spindle-shaped cells, which amounted to 1.12% +/- 0.58% (at 2 weeks) of the total cells in the CNVM. beta-gal expression was restricted to the CNVM, and there was no beta-gal transduction in surrounding normal retinochoroidal tissue. There was no correlation between choroidal **neovascularization** formation and beta-gal expression. CONCLUSIONS: The feasibility of gene transduction targeted to the photocoagulation-induced CNVM was demonstrated using **retroviral** vectors. By transducing functional genes, this model could be useful for investigating the possibility of **gene therapy** to inhibit formation of the CNVM in age-related macular degeneration.

L19 ANSWER 5 OF 21 MEDLINE on STN
AN 1998290229 MEDLINE
TI **Retrovirus**-mediated gene transfer targeted to retinal photocoagulation sites.
SO DIABETOLOGIA, (1998 May) 41 (5) 500-6.
Journal code: 0006777. ISSN: 0012-186X.
AU Murata T; Hoffmann S; Ishibashi T; Spee C; Gordon E M; Anderson W F; Hinton D R; Ryan S J
AB Diabetic retinopathy is a major cause of acquired blindness due to the development of retinal **neovascularization** and associated traction retinal detachment. It is commonly treated with retinal photocoagulation therapy; however, progression to blindness remains a significant problem. To determine the feasibility of adjunctive anti-**angiogenic gene therapy**, we evaluated the capability of **retroviral** vectors, which transfer exogenous genes only into dividing cells, to transfer and express a beta-galactosidase gene selectively into photocoagulation sites. Thirty-five rabbits received 30 retinal photocoagulation burns in the right **eye** followed 2 days later by beta-galactosidase (G1nBgSvNa) or control (G1XSvNa) vector injection into the subretinal space. Beta-galactosidase expression was observed in the photocoagulation sites from 5 days after vector administration (31.7+/-7.0%) to 12 weeks (6.7+/-3.4%). Immunohistochemical studies of the treated retinas using antibody Ber-MAC3 and anti-cytokeratin antibodies revealed that transduced cells were macrophages and retinal pigment epithelial cells. To determine feasibility in a primate, two monkeys received 10 laser burns in the macula superior to the fovea followed 2 days later by G1nBgSvNa vector. beta-galactosidase expression was found in photocoagulation sites and foveal retina was well preserved. We conclude that gene transfer to retinal photocoagulation sites provides stable expression of the transduced gene with relatively high efficiency. This feasibility study suggests the possibility of transferring genes encoding for anti-**angiogenic** factors into photocoagulation sites to improve the efficacy of laser photocoagulation therapy.

L19 ANSWER 6 OF 21 MEDLINE on STN
AN 1998202929 MEDLINE
TI Ability of **retroviral** transduction to modify the **angiogenic** characteristics of RPE cells.
SO GRAEFES ARCHIVE FOR CLINICAL AND EXPERIMENTAL OPHTHALMOLOGY, (1998 Mar) 236 (3) 220-9.
Journal code: 8205248. ISSN: 0721-832X.
AU Sakamoto T; Spee C; Scuric Z; Gordon E M; Hinton D R; Anderson W F; Ryan S J
AB BACKGROUND: Retinal pigment epithelial (RPE) cells play an important role in the modulation of **ocular angiogenesis**. Transduction of RPE cells with **retroviral** vectors bearing modulating genes can result in long-term transgene expression and may alter the **angiogenic** characteristics of RPE cells. This study was designed to determine whether changes in **angiogenic** characteristics of RPE cells result from transduction with **retroviral** vectors bearing modulating genes, using in vitro **angiog nic** assays, including analysis of endothelial proliferation

and wound healing. METHODS: Human RPE cells were transduced with **retroviral** vectors bearing either a urokinase-type plasminogen activator (u-PA) or a tissue-type plasminogen activator (t-PA) cDNA. Ten weeks after gene transfer, RPE cells transduced with the u-PA (u-PA-RPE cells) or the t-PA cDNA (t-PA-RPE cells), or untransduced (control) RPE cells, were cocultured with human umbilical vein endothelial cells (HUVECs) by contacting and non-contacting coculture methods. The effects of these cells on proliferation and in vitro "wound healing" of HUVECs were evaluated. RESULTS: Over 18 weeks, u-PA-RPE cells released large amounts of biologically active u-PA (total amount, 50.2 +/- 9.7 ng/10(6) cells/24 h), while t-PA-RPE cells released large amounts of functional t-PA (15.4 +/- 3.2 ng/10(6) cells/24 h). Control RPE cells did not release any detectable t-PA or u-PA. In the proliferation assay, u-PA-RPE cells stimulated HUVEC proliferation in contacting cell cultures, but not in non-contacting cell cultures. In contrast, t-PA-RPE cells, normal RPE cells or exogenous u-PA had no effect on HUVEC proliferation. In the wound healing assay, u-PA-RPE cells in contacting coculture and exogenous u-PA stimulated wound healing of HUVECs, while non-contacting u-PA-RPE cells, t-PA-RPE cells and normal RPE cells had no effect on HUVEC wound healing. RPE cells transduced with u-PA secreted large amounts of u-PA for as long as 18 weeks, and these cells stimulate HUVEC proliferation and in vitro wound healing. As a result, the **angiogenic** characteristics of RPE cells can undergo long-term changes. CONCLUSIONS: These results suggest that genetically modified RPE cells can be used to modulate **ocular angiogenesis** and may have potential for **gene therapy** of **ocular** diseases.

L19 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:464356 CAPLUS
DN 131:83970
TI Feline immunodeficiency virus gene therapy vectors
SO PCT Int. Appl., 170 pp.
CODEN: PIXXD2
IN Johnston, Julie C.; Sauter, Sybille L.; Hsu, David; Sheridan, Philip Lee; Hardy, Stephen F.; Dubensky, Thomas W.; Yee, Jiing-Kuan
AB Disclosed are gene therapy vectors based upon the feline immunodeficiency virus, as well as related packaging cell lines, methods for prodn., and methods of use.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9936511	A2	19990722	WO 1999-US1194	19990119
WO 9936511	A3	19990916		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002048805	A1	20020425	US 1999-231235	19990115
CA 2318575	AA	19990722	CA 1999-2318575	19990119
AU 9923295	A1	19990802	AU 1999-23295	19990119
EP 1045921	A2	20001025	EP 1999-903221	19990119
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 2003104611	A1	20030605	US 2001-872696	20010601

L19 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:354395 CAPLUS
DN 130:357142
TI Anti-**angiogenic** gene therapy vectors and their use in treating **angiogenesis**-related diseases
SO PCT Int. Appl., 83 pp.
CODEN: PIXXD2
IN Leboulch, Philippe; Pawliuk, Robert James; Bachelot, Thomas
AB A method for inhibiting tumor growth in a human patient harboring a solid tumor, said method comprising administering to said patient a nucleic acid mol. which expresses in said patient an anti-**angiogenic** polypeptide selected from the group consisting of human angiostatin,

murine angiostatin, human endostatin, murine endostatin, and **angiogenesis**-inhibiting fragments thereof, wherein expression of the anti-**angiogenic** polypeptide in the patient inhibits **angiogenesis** in the vicinity of the tumor and/or systemically by diffusion of the recombinant protein to the **vascular** compartment from secreting transduced cells, thereby inhibiting its growth.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9926480	A1	19990603	WO 1998-US24950	19981120
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9915985	A1	19990615	AU 1999-15985	19981120

L19 ANSWER 9 OF 21 MEDLINE on STN
AN 2000349651 MEDLINE
TI The possibility of gene therapy for the treatment of choroidal **neovascularization**.
SO OPHTHALMOLOGY, (2000 Jul) 107 (7) 1364-73.
Journal code: 7802443. ISSN: 0161-6420.
AU Murata T; Cui J; Taba K E; Oh J Y; Spee C; Hinton D R; Ryan S J
AB PURPOSE: Choroidal **neovascularization** (CNV) is responsible for most cases of severe visual loss in age-related macular degeneration. Recently, the possibility of **gene therapy** has been proposed for the treatment of CNV. The purpose of this study was to examine the feasibility of ex vivo and in situ **gene therapy** approaches for CNV. DESIGN: Experimental study. METHODS: Human retinal pigment epithelial (RPE) cells were transduced with a **retroviral** vector coding for beta-galactosidase. Transduced cells were grown on type II collagen sheets and transplanted under the retina of 20 rabbits. Animals were observed for 3 to 56 days, and transplanted cells were examined histologically and with X-gal staining. Bovine choroidal endothelial cells (CEC) were transduced with **retroviral** vectors coding for tissue inhibitor of metalloproteinase-2 (TIMP-2) or control vector. Production of TIMP-2 by transduced cells was determined by immunohistochemical analysis and enzyme-linked immunosorbent assay. Effect of transduction on in vitro proliferation, migration, and tube formation was examined in response to **vascular** endothelial growth factor (VEGF). Four CNV lesions were induced in one cynomolgus monkey by laser photocoagulation. Two days later, **retroviral** vector coding for TIMP-2 or control vector was injected into the subretinal space overlying the CNV lesions. The monkey was observed for 12 weeks using fluorescein angiography. RESULTS: Transplantation of transduced RPE cells was technically achieved in 10 of 20 animals. In these animals, RPE cells at the site of transplantation formed a monolayer and expressed beta-galactosidase for 14 days. beta-Galactosidase-positive cells were not identified at 56 days. Choroidal endothelial cells transduced with TIMP-2 secrete TIMP-2 into the media and show decreased migration and tube formation in vitro. In the in vivo monkey model, the control CNV lesions (n = 2) showed prominent leakage, whereas the experimental lesions (n = 2) showed minimal hyperfluorescence. CONCLUSIONS: **Retrovirally** transduced RPE cells survive in the subretinal space for at least 14 days and continue to express the gene product coded for by the vector. Choroidal endothelial cells **retrovirally** transduced for TIMP-2 produce TIMP-2 in vitro and show decreased **angiogenic** responses in vitro in response to VEGF. A preliminary study attempting in situ delivery of TIMP-2 vector to CNV lesions in a monkey **eye** supports the feasibility of this approach and encourages further study.

L19 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:666633 CAPLUS
DN 133:256758
TI Use of recombinant gene-delivery adeno-associated viral vectors for treating or preventing diseases of the eye

SO PCT Int. Appl., 86 pp.
CODEN: PIXXD2

IN Manning, William C., Jr.; Dwarki, Varavani J.; Rendahl, Katherine; Zhou, Shang-Zhen; McGee, Laura H.; Lau, Dana; Flannery, John G.; Miller, Sheldon; Wang, Fei; Di Polo, Adriana

AB Gene delivery vectors, such as, for example, recombinant adeno-assocd. viral vectors, and methods of using such vectors are provided for use in treating or preventing diseases of the eye.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000054813	A2	20000921	WO 2000-US7062	20000315
WO 2000054813	A3	20010503		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1183051	A2	20020306	EP 2000-916458	20000315
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002539176	T2	20021119	JP 2000-604885	20000315
US 2002194630	A1	20021219	US 2002-90983	20020304

L19 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:781135 CAPLUS
DN 135:330117
TI cDNAs encoding tubedown-1 and their use in treatment of ocular **neovascularization** and related diseases
SO PCT Int. Appl., 85 pp.
CODEN: PIXXD2
IN Gendron, Robert L.; Paradis, Helene
AB Tubedown-1 (tbdn-1), a protein assocd. with acetyltransferase activity has been characterized and its cDNA isolated. Tbdn-1 regulates endothelial differentiation through protein acetylation, DNA-binding or by interacting with and/or acetylating other protein targets important for endothelial differentiation. In normal adult eyes, tbdn-1 is expressed highly in the corneal endothelium proper and in the **vascular** endothelium of the limbus and retina. Tbdn-1 is absent or down regulated in the **vascular** endothelia of diseased and injured eyes, including eyes from patients with proliferative retinopathies involving **neovascularization**. Inhibition of tbdn-1 expression in endothelial cells in vitro indicates tbdn-1 acts as an inhibitor of **angiogenesis**. Thus, high levels of tbdn-1 expression present in normal ocular endothelial cells is assocd. with suppression of abnormal **neovascularization** in the eye demonstrating the therapeutic usefulness of tbdn-1 as a regulator of retinal **angiogenesis**. The present invention provides methods for treating, inhibiting or delaying the onset of **angiogenesis**-assocd. diseases like diabetic retinopathy, retinopathy of prematurity, primary hyperplastic vitreous, macular degeneration and other conditions involving ocular **neovascularization**.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001079506	A2	20011025	WO 2001-US12548	20010417
WO 2001079506	A3	20020314		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002137678	A1	20020926	US 2001-836503	20010417

L19 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:507557 CAPLUS
DN 135:106034
TI Gene therapy of corneal **neovascularization** with genes for anti-**angiogenic** factors
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
IN Abitbol, Marc
AB Methods of preventing corneal **neovascularization** using vectors carrying genes for anti-**angiogenic** factors such as angiostatin or endostatin are described. Factors including angiostatin, angiostatin K3, the N-terminal fragment of urokinase (ATF), endostatin, and platelet factor 4 may be used. The use of an adenovirus vector to transfer a reporter gene into the cornea is demonstrated. Adenovirus vectors carrying ATF or angiostatin K3 genes were able to prevent **neovascularization** of sutured corneas without either inducing inflammation or causing regression of limbic **vascularization**.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001049316	A2	20010712	WO 2000-FR3653	20001221
WO 2001049316	A3	20020523		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2803207	A1	20010706	FR 1999-16780	19991230
EP 1246642	A2	20021009	EP 2000-993688	20001221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003170209	A1	20030911	US 2003-169180	20030304

L19 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:319735 CAPLUS
DN 134:348295
TI Ribozyme therapy for the treatment of proliferative skin and eye diseases
SO PCT Int. Appl., 408 pp.
CODEN: PIXXD2
IN Robbins, Joan M.; Tritz, Richard
AB As an effective therapy for proliferative skin and eye diseases, e.g. psoriasis and proliferative diabetic retinopathy, the invention provides ribozymes and ribozyme delivery systems which cleave RNA encoding cytokines involved in inflammation, matrix metalloproteinases, a cyclin, a cell-cycle dependent kinase, a growth factor, or a reductase.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001030362	A2	20010503	WO 2000-US29500	20001026
WO 2001030362	A3	20020117		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1223950	A2	20020724	EP 2000-975399	20001026
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003530309	T2	20031014	JP 2001-532780	20001026

L19 ANSWER 14 OF 21 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AN 2002:548194 SCISEARCH
TI Gene therapy for retinal and choroidal diseases
SO EXPERT OPINION ON BIOLOGICAL THERAPY, (JUN 2002) Vol. 2, No. 5, pp.

537-544.
Publisher: ASHLEY PUBLICATIONS LTD, UNITEC HOUSE, 3RD FL, 2 ALBERT PLACE, FINCHLEY CENTRAL, LONDON N3 1QB, ENGLAND.
ISSN: 1471-2598.
AU Campochiaro P A (Reprint)
AB The **eye** is a small compartment separated from the systemic circulation by the blood-**ocular** barriers, providing advantages for **intraocular** gene transfer - an approach which is being investigated for several types of retinal and choroidal diseases. A compelling application is gene replacement for homozygous loss-of-function mutations in genes differentially expressed in photoreceptors or retinal pigmented epithelial (RPE) cells that result in retinal degeneration. Considerable progress has been made in this area, including demonstration of return of visual function in RPE65(-/-) dogs after subretinal injection of adeno-associated viral vectors encoding RPE65, providing groundwork for a clinical trial in patients with Leber's Congenital Amaurosis. Proof of principle has been provided for **intraocular** gene transfer of ribozymes for dominantly inherited retinal degenerations. Survival factor **gene therapy** shows promise for treatments that may be used in multiple retinal degenerations. Transduction of **intraocular** and/or periocular cells with constructs that encode antiangiogenic proteins provides a new approach for sustained local delivery treatment of retinal and choroidal **neovascularisation**. While considerable investigation remains to work out critical details, there is substantial evidence suggesting that in the near future, **gene therapy**-based treatments will be an important addition to what is currently offered to patients with retinal and/or choroidal diseases.

=> d an ti so au ab pi l20 6 5 4 2

L20 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:334392 CAPLUS
DN 138:348751
TI Lentiviral vector-mediated gene transfer and uses thereof
SO U.S. Pat. Appl. Publ., 61 pp., Cont.-in-part of U. S. Ser. No. 25,264.
CODEN: USXXCO
IN Appukuttan, Binoy; Stout, J. Timothy
AB The present invention provides lentiviral vectors that are useful in human gene therapy for inherited or acquired proliferative ocular disease. It furnishes methods to exploit the ability of lentiviral vectors to transduce both mitotically active and inactive cells so that eye diseases may be treated.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2003082159	A1	20030501	US 2002-245050	20020917
US 2002114783	A1	20020822	US 2001-25264	20011219

L20 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:487422 CAPLUS
DN 137:57587
TI Lentiviral vector-mediated gene transfer and uses thereof
SO PCT Int. Appl., 91 pp.
CODEN: PIXXD2
IN Stout, J. Timothy; Appukuttan, Binoy
AB The present invention provides a means of human gene therapy for inherited or acquired proliferative ocular disease. It furnishes methods to exploit the ability of lentiviral vectors to transduce both mitotically active and inactive cells so that eye diseases may be treated.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002049677	A1	20020627	WO 2001-US49241	20011218

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,

CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002034053	A5	20020701	AU 2002-34053	20011218
EP 1343532	A1	20030917	EP 2001-985065	20011218

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

L20 ANSWER 4 OF 6 MEDLINE on STN
AN 2002132046 MEDLINE
TI IL-12 suppresses the expression of **ocular** immunoinflammatory lesions by effects on **angiogenesis**.
SO JOURNAL OF LEUKOCYTE BIOLOGY, (2002 Mar) 71 (3) 469-76.
Journal code: 8405628. ISSN: 0741-5400.
AU Lee Sujin; Zheng Mei; Deshpande Shilpa; Eo Seong Kug; Hamilton Thomas A; Rouse Barry T
AB Topical application of plasmid DNA encoding IL-12 to the cornea of mice prior to **ocular** infection with Herpes simplex virus type 1 (HSV) results in diminished corneal immunoinflammatory lesions. Such herpetic stromal keratitis (HSK) reactions in humans represent an important cause of blindness. The effect of IL-12 pretreatment acted via inhibitory effects on corneal **neovascularization** rather than by inhibiting viral replication or the function of CD4(+) T cells that mediate HSK. The antiangiogenesis induced by IL-12 DNA application was mediated indirectly via the cytokine IFN-gamma and one or both of two chemokine molecules, **IP-10** and **MIG**. Thus IL-12 DNA administration lacked modulatory effects on HSK in GKO mice, indicating the necessary involvement of IFN-gamma induction for antiangiogenesis. In contrast, exposure of GKO mice to **IP-10** DNA did suppress the severity of HSK. Furthermore, treatment with specific antisera to **IP-10** and **MIG** in HSV-infected mice abrogated the IL-12-induced inhibitory effect on lesion severity. Taken together, our data indicate that the HSV-induced **ocular** immunoinflammatory lesions can be modulated by IL-12 and that this effect results from chemokine inhibition of **angiogenesis**. The use of antiangiogenesis therapy might represent a useful control measure against HSK.

L20 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:761116 CAPLUS
DN 131:350279
TI **Interferon-inducible** protein 10 is a potent inhibitor of angiogenesis
SO U.S., 29 pp.
CODEN: USXXAM
IN Tosato, Giovanna; Angiolillo, Anne L.; Sgadari, Cecilia
AB The authors disclose that **interferon-inducible** protein 10 is a potent inhibitor of angiogenesis. The present invention claims the use of **interferon-inducible** protein 10 (**IP-10**) as well as fragments and analogs for therapeutic application in angiogenesis-assocd. disorders. In one example, **IP-10** inhibited basic fibroblast growth factor-induced neovascularization in immunocompromised mammals. In addn., **IP-10** was shown to suppress endothelial cell differentiation into tubular capillary structures.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5994292	A	19991130	US 1995-455079	19950531